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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/560,803	04/28/2000	Won-Bin Young	P04014US1	5114

22885 7590 02/23/2004

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/560,803	YOUNG ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-13,15-29, 31-39* is/are pending in the application.

4a) Of the above claim(s) *11-13,15-25,34 and 36-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-10, 26-29, 31-33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed November 26, 2003 in response to the Office Action of August 27, 2003 is acknowledged and has been entered. Claims 1, 2, 4-10, 26-29, 31-33 and 35 are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

The rejection of claim 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite **is withdrawn** in view of Applicant's amendment to the claims.

The rejection of claims 26-29, 31-33 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is maintained** for reasons of record.

Claim 26, is indefinite in the recitation of "a method of increasing the presence of viral titer" because the endpoint(s) of claimed methods are ambiguous and unclear. There is an absence or lack of clarity as to critical or resolutions steps or endpoints which reads back on the preamble of the claimed methods. Claims 26, furthermore does not set out positive method steps to achieve the claimed method of "method of increasing the presence of viral titer". Clarification of the specific method steps envisioned by the instant claim is required.

The rejection of claims 10 and 32 for containing the trademark/trade name Zeocin™ **is maintained**. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. In the present case, the trademark/trade name is used to identify/describe a special formulation containing Phleomycin D1 and, accordingly, the identification/description is indefinite. Applicant's have amended the claims, however, the claim amendment still does not comply with the requirements set out in MPEP 608.01 (v).

> The examiner should not permit the use of language such as "the product X (a descriptive name) commonly known as Y (trademark)" since such language does not bring out the fact that the latter is a trademark. Language such as "the product X (a descriptive name) sold under the trademark Y" is permissible.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 2, 4, 6-9, 26-29, 31 and 35 under 35 U.S.C. 102(e) being anticipated by Beach et al. (U.S Pat. No. 6,025,192) or (U.S. Pat. No. 6,255,071) **is maintained** for reasons of record.

Applicant's arguments have been fully considered but are not deemed persuasive. Applicant's arguments are focused on the difference in viral titer production between the cited art and the instant invention. Applicant's provide theoretical arguments on reason why this may be the case. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. specific RNA export sequences not found in the cited art; cell line with very low copy number of stably integrated chromosomal copies of the helper vector and the transfer vector; sustained helper

virus gene expression which would increase virion production) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The instant invention is drawn to a method of establishing a vector packing cell, by introducing a helper virus into the cell population. The term "helper virus" is interpreted to be (specification page 8 lines 14-30):

> A plasmid that enables positive selection of cells with active helper virus. More particularly an internal ribosome entry site along with a marker selection gene downstream of the *gag, pol,* and *env* genes provided positive selection of helper virus which had not been inactivated by methylation. "Helper virus" shall include any packaging deficient vector or nucleotide sequence encoding a viral protein, the expression of which is necessary in a vector producing cell for assembly an packaging of a particular vector capsid.

A viral vector containing a gene of interest is added to the cell containing the helper virus. The term "viral vector" is interpreted to be (specification page 9 lines 18-31):

> Viral vector shall include any viral based vector which embodies less than all structural proteins necessary for viral capsid assembly, and any additional nucleotide sequences desirable for expression or to be delivered to; a host cell. The instant invention utilizes the term "comprising" which can include more additional steps additional steps.

The selection of non-methylated helper virus is achieved by providing the selection pressure with an antibiotic (claims 1, 2, 4, 26, 27, 29 and 35). The presence of an LTR linked to a viral production gene is sufficient to be "capable of being methylated".

Beach et al. disclose the production of a retroviral vector packaging cell line (see section 5.6, U.S Pat. No. 6,025,192, columns 9-11 or U.S. Pat. No. 6,255,071, columns 17-21). The reference indicates the use of a polycistronic packaging cassette comprising at least two genes

sequences important for efficient packaging of retroviral derived nucleic acid into functional retroviral particles in operative association with a selectable marker and a quantifiable marker. The polycistronic expression cassettes allows for the selection of the selectable marker which ensures that only those cells expressing the gene sequence important for packaging are selected. The retroviral packaging cell lines of the reference optimize expression from retroviral LTR promoters (capable of being methylated). The packing cell lines can be developed which express gag, pol and or env proteins modified in a manner that promotes an increased viral titer an/or infectivity range (see also section 13.2-13.5, U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071, columns 45-47). The reference discloses the production of a packing cell that provides gag, pol and/or env sequences which are then linked to an IRES linked to a selection maker in this case hygromycin (see figure 18 of U.S. Pat. No. 6,255,071). The reference also discloses a viral vector comprising a packing sequence containing a polylinker cloning site and an IRES with a selection marker (see figure 1 of , U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071). Therefore, the instant invention is anticipated by Beach et al.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 2, 4-10, 26-29, 31 and 35 under 35 U.S.C. 103(a) being obvious Beach et al. (U.S Pat. No. 6,025,192) or (U.S. Pat. No. 6,255,071) **is maintained** for reasons of record.

Applicant's arguments have been fully considered but are not deemed persuasive. Applicant's arguments are focused on the difference in viral titer production between the cited art and the instant invention. Applicant's provide theoretical arguments on reason why this may

be the case. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. specific RNA export sequences not found in the cited art; cell line with very low copy number of stably integrated chromosomal copies of the helper vector and the transfer vector; sustained helper virus gene expression which would increase virion production) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The instant invention is now drawn to a method of establishing a vector packing cell, by introducing a helper virus into the cell population. The term "helper virus" is interpreted is defined in the specification page 8 lines 14-30. A viral vector containing a gene of interest is added to the cell containing the helper virus. The term "viral vector" is defined in the specification on page 9 lines 18-31. The selection of non-methylated helper virus is achieved by providing the selection pressure with an antibiotic (claims 1, 2, 4, 26, 27, 29 and 35). The presence of an LTR linked to a viral production gene is sufficient to be "capable of being methylated".

Beach et al. teach the production of a retroviral vector packaging cell line (see section 5.6, U.S Pat. No. 6,025,192, columns 9-11 or U.S. Pat. No. 6,255,071, columns 17-21). The reference teaches the use of a polycistronic packaging cassette comprising at least two genes sequences important for efficient packaging of retroviral derived nucleic acid into functional retroviral particles in operative association with a selectable marker and a quantifiable marker. The polycistronic expression cassettes allows for the selection of the selectable marker which

ensures that only those cells expressing the gene sequence important for packaging are selected. The novel retroviral packaging cell lines of the invention optimize expression from retroviral LTR promoters (capable of being methylated). The packing cell lines can be developed which express gag, pol and or env proteins modified in a manner that promotes an increased viral titer an/or infectivity range (see also section 13.2-13.5, U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071, columns 45-47). The reference teaches the production of a packing cell that provides gag, pol and/or env sequences which are then linked to an IRES linked to a selection maker in this case hygromycin (see figure 18 of U.S. Pat. No. 6,255,071). The reference also teaches a viral vector comprising a packing sequence containing a polylinker cloning site and an IRES with a selection marker (see figure 1 of , U.S Pat. No. 6,025,192, columns 35-38 or U.S. Pat. No. 6,255,071).

The reference does not teach using the Ziocin as the selection marker in the helper virus construct. It would have been *prima facie* obvious to utilize any known mammalian antibiotic resistance marker that is functional in a mammalian cell as suggested by Beach et al. (see U.S Pat. No. 6,025,192, column 4, lines 4-9). Zeocin (a.k.a. Pleomycin) resistance gene is a well-known and characterized protein in the art, it is known to be is non-toxic in a wide variety of cells and is a known antibiotic used for selection in mammalian cell culture. The advantage of using Zeocin is that the same antibiotic can be used in a bacterial culture and a mammalian cell culture. Beach et al. provides the motivation by suggesting the use of any antibiotic which can function as a mammalian marker. Therefore, the instant invention is obvious over Beach et al.

Conclusion

Claims 1, 2, 4-10, 26-29, 31-33 and 35 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 or for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER

2/20/04